Pseudoneutropenia from EDTA Leukoagglutination

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Dear Editor:

Pseudo-neutropenia is a rare phenomenon and has no physiologic consequences,1-7 however, it may lead to multiple unnecessary tests if not recognized.8 A 20-year-old woman with no significant past medical history presented to her primary care physician with symptoms of an upper respiratory tract infection. Complete blood count (CBC) performed the same day revealed a white blood cell (WBC) count of 3.7×10⁹/L with a differential of 53% neutrophils, 30% lymphocytes, 17% monocytes and less than 1% eosinophils and basophils; hemoglobin of 12.6 g/mL and platelet count of 168×10⁹/L. The patient completed a course of azithromycin with resolution of her symptoms. Two weeks after the first CBC, a repeat CBC was obtained to monitor her WBC. This second test revealed a WBC count of 3.6×10⁹/L with no changes in the other parameters. The patient was referred to a hematologist for further evaluation of her apparent neutropenia.

On further questioning, the patient denied repeated infections, easy bruising, known bleeding disorders, joint pain or skin rash. She recalled being told that she had a low WBC as a child but no documentation of prior blood counts was available. She had prior orthopedic surgery after a sports injury with no complications. Her only medications other than azithromycin were ibuprofen during her acute illness and a one-year use of drospirenone/ethinyl estradiol (Yasmin) for contraception. She had no known history of HIV, hepatitis B or C viruses. The patient denied histories of smoking, alcohol use or intravenous drug use. Family history was significant for a father with hypertension, non-insulin-dependent diabetes mellitus and coronary artery disease; her mother had hypertension. A family history of connective tissue disorders, leukemia and lymphoma was specifically denied. Physical exam revealed no lymphadenopathy or hepatosplenomegaly.

Further lab studies included ANA, ANCA, HIV and a Monospot test,
which were negative. Vitamin B12 and folic acid levels were within normal limits. A third CBC revealed a WBC of 2.7×10⁹/L four weeks after the initial study. Peripheral smear showed an adequate number of white cells which were arranged in clumps (Figure 1A). The patient was asked to return the next day for repeat testing. At this time, blood samples for CBC were collected in a prewarmed EDTA tube and a citrate tube (Figure 1B, C). White blood cell counts from both tubes were within normal limits at around 5200/mm³.

The final impression was a completely artificial low WBC due to antibodies causing neutrophil agglutination only in the presence of EDTA at cold temperatures.

References

Figure 1. Peripheral smear. Clumping of leukocytes in an EDTA tube (A). Agglutination resolved when blood was drawn in a prewarmed EDTA tube (B) or a citrate tube (C).